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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FORD, ALLISON M	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 07/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,877	O'LOUGHLIN ET AL.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-98* is/are pending in the application.

4a) Of the above claim(s) *26-39,49-61,70-85,97 and 98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25,40-48,62-69 and 86-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-25, 40-48, 62-69, and 86-96, in the reply filed on 13 June 2005 is acknowledged. The traversal is on the ground(s) that a single search and examination covering all claims would not place undue burden on the Examiner. This is not found persuasive because burden consists not only of specific searching of classes and subclasses, but also of searching multiple databases for foreign references and literature searches. Burden also resides in the examination of independent claim sets for clarity, enablement and double patenting issues. Therefore searching the instant five patentably distinct inventions would, in fact, impose a serious burden on the examiner. The requirement is still deemed proper and is therefore made FINAL.

Status of Application

Applicant's arguments filed 13 June 2005 have been fully considered but they are not persuasive. Amendments to claims 1, 8, and 86 have been entered. Claims 1-98 remain pending in the current application, of which claims 26-39, 49-61, 70-85 and 97-98 are withdrawn from consideration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6 and 7 remain rejected under 35 U.S.C. 102(b) as being anticipated by Marquisee (US Patent 3,954,678).

Marquisee teaches a semipermeable microcapsule which comprises silica gel within a semipermeable membrane. The capsule can contain a biological catalyst, preferably urease or urate oxidase (uricase) (See col. 2, ln 38-57) (Claim 1). The membrane is impermeable to these enzymes, therefore the enzymes cannot be released externally of the capsule (See col. 2, ln 29-37) (Claim 6). Additional auxiliary cell stabilizing agents can be added to the silica gel to allow for normal separation and purification of the microcapsule without cell collapse, such agents can include alginate (See col. 2, ln 1-10) (Claim 7). Though Marquisee does not specifically teach the semipermeable microcapsules to be used for oral delivery, the oral delivery composition as claimed is the same as that taught in the prior art, therefore the semipermeable microcapsule of Marquisee is considered one and the same as the oral delivery composition as in the current application; therefore the reference anticipates the subject matter.

In response to the rejection of claims 1, 6 and 7 under 102(b) as being anticipated by Marquisee, applicants argue that Marquisee does not disclose or suggest an oral delivery device composition, as in claim 1. Absent such disclosure or suggestion applicants do not believe the composition described by Marquisee could be taken as orally as an oral delivery composition.

This is not found persuasive because, as stated above, it is recognized that Marquisee does not specifically suggest using the semipermeable microcapsule, which comprises silica gel and a biological catalyst, preferably urease or urate oxidase (uricase) (See Marquisee col. 2, ln 38-57), as an oral delivery device, the composition of Marquisee is the same as currently claimed. Therefore, though Marquisee discloses different intended uses for their composition, the nature and make-up of the composition is one and the same as the oral delivery composition as currently claimed; and therefore has the same inherent functions, including use as an oral delivery composition. Applicants have provided not evidence or reasoning as to why the composition of Marquisee cannot be used as an oral delivery device; therefore,

despite non-disclosure of that particular use in the Marquisee reference, the compositions are considered to be one and the same.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-8, 10-17, 25, 40-45, 47-48, 62-66, 68-69, 86-91 and 93-96 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al (US Patent 6,217,859), in view of Setala (US Patent 4,022,883), and further in view of Yamamoto et al (US Patent 5,627,065) and Shigyo et al (US Patent 5,728,562) and in light of The Online Medical Dictionary.

Chang et al teach an article comprising an oral delivery composition, comprising a microencapsulated genetically engineered microorganism in a pharmaceutically acceptable carrier (which applicant calls a capsule comprising at least one cell transfected with a gene) (See Chang et al, col. 2, ln 24-31). The microencapsulating material can be an alginate-polylysine-alginate (See col. 2, ln 38-45). The microencapsulating material is able to entrap the microorganisms so that the microorganisms are not released externally from the capsule, but does not impede mass transport of the undesirable molecules for removal to enter in contact with the entrapped microorganisms (See col. 2, ln 46-52). In a preferred embodiment Chang et al teach encapsulating genetically engineered *E.coli* DH5 cells, which are transfected with the urease gene from *Klebsiella aerogens*, for the purpose of urea removal (See col. 3, ln 58- col. 4, ln 40 & Claim 9).

Though Chang et al only teach transfecting a cell with the urease gene, for the purpose of urea removal in uremic patients, it would have been obvious to one of ordinary skill in the art at the time the

invention was made to additionally transfect the cell with the uricase and creatininase genes in addition to the urease gene. One of ordinary skill in the art would have been motivated to use cells transfected with uricase, creatininase and urease genes so the cell would produce uricase, creatininase and urease. Uric acid, creatine and urea are all uremic toxins that accumulate in uremic patients (See Setala, col. 3, ln 18-36). Uricase, creatininase and urease break down uric acid, creatine and urea, respectively, to more dilute compounds which can be excreted in the urine (See The Online Medical Dictionary "Uricase," "Allantoin," "Creatininase," "Creatinine" and "Urea"). Therefore, one of ordinary skill in the art would have been motivated to use a cell transfected with uricase, creatininase and urease, encapsulated in the microcapsule taught by Chang et al, in order to aide in the breakdown and removal of three uremic toxins that accumulate in uremic patients. One would have expected success transfecting a cell with the uricase gene because Shigyo et al teach isolation of the uricase gene from Bacillus sp. and subsequent transfection into and expression in *E.coli* cells (See Shigyo et al, col. 6, ln 15- col. 8, ln 34). One would have expected success transfecting a cell with the creatininase (creatinine amidohydrolase) gene because Yamamoto et al teach isolation of the creatininase gene from *Pseudomonas putida* PS-7 and subsequent transfection into and expression in *E.coli* cells (See Yamamoto et al, col. 3, ln 6-57 & Claim 5). One would have expected the transfected cells encapsulated in the microcapsule of Chang et al to successfully secrete all three enzymes because Chang et al teach a genetically engineered cell, transfected with urease, successfully secreted the urease enzyme in levels that were sufficient to lower urea levels in uremic patients (See col. 8, ln. 38- col.9, ln 5). Uricase and creatininase are known to break down uric acid and creatine, respectively, therefore one of ordinary skill in the art would expect similar success removing uric acid and creatine when uricase and creatininase are delivered to the gastrointestinal tract of a uremic patient (Claim 40, 42, 44-45 and 47). Therefore the microencapsulated cell of Chang et al is an effective delivery device capable of delivering all three gene product enzymes to remove the three uremic toxins.

Alternatively, it would have been obvious to one of ordinary skill in the art to encapsulate multiple cells using the method of Chang et al, wherein a first cell is transfected with only urease, a second cell is transfected with only creatininase, and a third cell is transfected with only uricase (Claims 41 and 43). Still further, multiple cells could be transfected with the three genes in any combination of ways, wherein a first cell is transfected with two of the genes of interest, and a third cell is transfected with only the remaining third gene of interest. Any order and combination of genes transfected into a single cell or multiple cells would be obvious to one of ordinary skill in the art, as long as all three genes were present within the microcapsule taught by Chang et al because Chang et al does encapsulate multiple cells (See col.4, ln 41-64). One of ordinary skill in the art would have been motivated to manipulate the order and combination of genes transfected into single or multiple cells based on the availability of transformed cells, if purchased commercially, or if made in the laboratory, based on the transfection vectors used, as some vectors may contain two of the genes, allowing them to be activated by a single promoter, while a third gene may be contained on a separate vector that is induced by a separate promoter. The combination of the genes of interests in a single or in multiple cells would be an obvious choice of experimental design. The order and combination of the genes encoding the enzymes, whether they be in a single or multiple cells, will not effect the efficiency of the article, as all genes will be expressed, and therefore all three enzymes will be present in the microcapsule; therefore one would expect equal levels of success no matter what order or combination the genes are transfected in the cells.

Still further, though Chang et al, Shigyo et al and Yamamoto et al teach examples wherein the urease, uricase and creatininase genes were transfected into *E.coli* cells, respectively, it would have been obvious to one of ordinary skill in the art to use any suitable microorganism as the host cell in which to transfect the three genes of interest (Claims 64-66 and 68). The choice of host microorganism would have been a matter of experimental design choice; any suitable, biocompatible bacteria that can easily be genetically engineered would have been suitable. One of ordinary skill in the art would have been

motivated to use any suitable microorganism because Chang et al teach that any suitable microorganism can be used in accordance with their invention, including, for example, *Bacillus pastteuri* (See Chang et al col. 3, ln 58-65). One would have expected success because one of ordinary skill in the art would be able to select a microorganism suitable for transfection and in vivo use, as methods of transfection are well known in the art (See, e.g. Shigyo et al and Yamamoto et al), and Chang et al teach a general method of encapsulation that is applicable to multiple cell types.

Alternatively, instead of encapsulating the entire genetically engineered cell, as in the method of Chang et al, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the oral delivery composition of Chang et al to comprise a microcapsule comprising isolated urease, uricase and creatinase, instead of cells transfected with the genes for urease, uricase and creatinase, as described above (Claims 1-4, 6-8, 25, 86-91 and 93). One of ordinary skill in the art would have been motivated to encapsulate isolated enzymes, instead of whole cells, because isolated enzymes can be easily purchased from commercial sources, are less complicated in terms of biocompatibility, immune reactions and overall safety than genetically modified organisms, isolated enzymes require less effort in storage, packaging and transportation, and compositions comprising isolated enzymes are easier to get approved by the FDA than genetically modified organisms. One would have expected success because isolated urease, creatininase and uricase enzymes would have the same effect on breaking down urea, creatine and uric acid, respectively, as enzymes produced by cells transfected with the same genes since the active product is the same; therefore would one would have expected the same level of success as was obtained using transfected cells, as taught above. Furthermore, because isolated urease, creatininase and uricase encapsulated in the microcapsule of Chang et al would have the same effect as the enzymes encoded for by the encapsulated transfected cells, it would further have been obvious to encapsulate both cells (either *E.coli* or any other suitable microorganism, see teachings above) transfected with the genes for urease, creatininase and uricase, and isolated urease, creatininase and uricase because

combining two compositions that have the same effect to create a third composition with the same effect as the first two, is prima facie obvious. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). The combination of isolated enzymes and enzymes encoded for by transfected cells would only strengthen the degradation of the uremic toxins in the uremic patient's system (Claims 10-17, 48, 69 and 94-96).

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 5 and 9 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al (US Patent 6,217,859), in view of Setala (US Patent 4,022,883), further in view of Yamamoto et al (US Patent 5,627,065) and Shigyo et al (US Patent 5,728,562), and still further in light of The Online Medical Dictionary and Merriam-Webster Online Dictionary.

Chang et al teach an article comprising an oral delivery composition, comprising a microencapsulated genetically engineered microorganism in a pharmaceutically acceptable carrier (which applicant calls a capsule comprising at least one cell transfected with a gene) (See Chang et al, col. 2, ln 24-31). In a preferred embodiment Chang et al teach encapsulating genetically engineered *E.coli* DH5 cells, which are transfected with the urease gene from *Klebsiella aerogens*, for the purpose of urea removal (See col. 3, ln 58- col. 4, ln 40 & Claim 9).

It would have been obvious for the oral delivery composition of Chang et al to comprise a microcapsule comprising isolated urease, uricase and creatinase, as taught above.

Though Chang et al is silent on the presence of an enteric coating on the microcapsules, as well as the microcapsules resistance to acid degradation, it would have been obvious to one of ordinary skill in the art at the time the invention was made to enterically coat the modified capsule of Chang et al (modified to comprise isolated urease, uricase and creatininase), in order to protect the capsule from acid

degradation in the stomach so that it may pass, unaltered, into the intestines where it will function to degrade the uremic toxins. By definition, an enteric coating is designed to pass through the stomach, unaffected by the gastric juices and acids, to disintegrate in the intestines (See Merriam-Webster Online Dictionary). Chang et al do state that the microcapsules are to function in the intestines (See col. 3, ln 26-39); therefore one of ordinary skill in the art would have been motivated to enterically coat the microcapsules to protect them from acid degradation in the stomach, allowing unaltered passage to the intestines, where they will act to degrade the uremic toxins (Claims 5 and 9). One would have expected success because enteric coating of capsules and other medicinal preparations for the purpose of protection from acid degradation is well known to one of ordinary skill in the art. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 18-21, 46, 67 and 92 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al (US Patent 6,217,859), in view of Setala (US Patent 4,022,883), further in view of Yamamoto et al (US Patent 5,627,065) and Shigyo et al (US Patent 5,728,562), and still further in view of Sparks et al (Trans. Am. Soc. Artif. Intern. Org, 1972) and Wolfe et al (The International Journal of Artificial Organs, 1987), and in light of The Online Medical Dictionary.

Chang et al teach an article comprising an oral delivery composition, comprising a microencapsulated genetically engineered microorganism in a pharmaceutically acceptable carrier (which applicant calls a capsule comprising at least one cell transfected with a gene) (See Chang et al, col. 2, ln 24-31). In a preferred embodiment Chang et al teach encapsulating genetically engineered *E.coli* DH5 cells, which are transfected with the urease gene from *Klebsiella aerogens*, for the purpose of urea removal (See col. 3, ln 58- col. 4, ln 40 & Claim 9).

It would have been obvious for the oral delivery composition of Chang et al to comprise a cell that is additionally transfected with the uricase and creatininase genes in addition to the urease gene, as taught above. Though Chang et al uses an *E.coli* cell, it would have been obvious to use a cell that is not *E. coli*, as taught above. Additionally, it would have been obvious for the oral delivery composition of Chang et al to comprise a microcapsule comprising isolated urease, uricase and creatinase, thus the cell would contain at least two isolated uremic enzymes, as taught above.

Chang et al does not teach including an ammonium uptake species in the capsule; however, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include an ammonium uptake species in the capsules. Such ammonium uptake species include zirconium phosphate (See Kominami et al, col. 5, ln 51-66 & Wolfe et al, Pg. 269), activated carbon (See Kominami et al, col. 5, ln 51-66) and oxidized starch (which applicant calls oxystarch) (See Sparks et al, Pg. 459) (Claims 18-21, 46, 67 and 92). Kominami et al, Wolfe et al and Sparks et al have all shown zirconium phosphate, activated carbon and oxidized starch to be suitable sorbents for the adsorption of ammonia, which is formed by the breakdown of urea by urease (See The Online Medical Dictionary, "Urease"). Therefore one of ordinary skill in the art would have been motivated to include at least one of zirconium phosphate, activated carbon and oxidized starch in the modified microcapsules of Chang et al in order to adsorb the excess ammonia created by the breakdown of urea. One would have expected success because zirconium phosphate, activated carbon and oxidized starch are all taught to adsorb ammonia (See Kominami et al, Wolfe et al and Sparks et al). Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 22-24, 46, 67 and 92 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al (US Patent 6,217,859), in view of Setala (US Patent 4,022,883), further in view of Yamamoto

et al (US Patent 5,627,065) and Shigyo et al (US Patent 5,728,562), and still further in view of Smith et al (US Patent 4,857,555) and in light of The Online Medical Dictionary.

Chang et al teach an article comprising an oral delivery composition, comprising a microencapsulated genetically engineered microorganism in a pharmaceutically acceptable carrier (which applicant calls a capsule comprising at least one cell transfected with a gene) (See Chang et al, col. 2, ln 24-31). In a preferred embodiment Chang et al teach encapsulating genetically engineered *E.coli* DH5 cells, which are transfected with the urease gene from *Klebsiella aerogens*, for the purpose of urea removal (See col. 3, ln 58- col. 4, ln 40 & Claim 9).

It would have been obvious for the oral delivery composition of Chang et al to comprise a microcapsule comprising isolated urease, uricase and creatinase, as taught above.

Chang et al does not teach including an ammonium uptake species in the capsule; however, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include an ammonium uptake species in the capsules, such as glutamine synthetase (which applicant calls an ammonium uptake species). Smith et al teach that glutamine synthetase is responsible for catalyzing the synthesis of glutamine from glutamate and ammonia (See Smith et al, col. 1, ln 34-50); the glutamine produced by this reaction is readily used by the body in a variety of natural ways. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include glutamine synthetase in the modified microcapsule of Chang et al (Claims 22-24, 46, 67 and 92). One would have been motivated to include glutamine synthetase in the modified microcapsule of Chang et al in order to naturally utilize the excess ammonia produced by the break down of urease to synthesize glutamine, a naturally occurring amino acid that aides the body naturally. One would have expected success because Smith et al teach that glutamine synthetase catalyzes the reaction of glutamate and ammonia to form glutamine, which can then forth be utilized directly in the gastrointestinal tract as

respiratory fuel (See Smith et al, col. 1, ln 34-col. 2, ln 2). Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

The examiner thanks applicant for pointing out the typographical error in the listing of the rejected claims; as presumed by applicant, claims 1-4, 6-8, 10-17, 25, 40-45, 47, 48, 62-66, 68, 69, 86-91 and 93-96 were originally rejected under 35 U.S.C. § 103(a) as being unpatentable over Chang et al (US Patent 6,217,859), in view of Setala (US Patent 4,022,883), and further in view of Yamamoto et al (US Patent 5,627,065) and Shigyo et al (US Patent 5,728,562) and in light of The Online Medical Dictionary (http://cancerweb.ncl.ac.uk/cgi-bin/omd, accessed 2/28/05).

In response to the rejection under 103(a) of independent claims 1 and 86 as being unpatentable over Chang et al, in view of Setala, further in view of Yamamoto et al and Shigyo et al, and in light of The Online Medical Dictionary, applicant argues that none of the references disclose or suggest use of an isolated uricase and isolated creatininase, as recited in claim 1, or an isolated uremic enzyme, as recited in claim 86. Rather, applicant argues both Chang et al and Setala describe various microorganisms and teach that a microorganism is required, but do not disclose or suggest an isolated enzyme; therefore Chang et al and Setala teach away from use of an isolated enzyme.

This is not found persuasive because both Chang et al and Setala teach that the function of the microorganisms is to secrete the uremic enzymes; therefore the functional elements are the uremic enzymes, per se, not the microorganisms (See Chang et al, col. 5, ln 65-col. 6, ln 9). Therefore, as stated previously, it would have been obvious to one of ordinary skill in the art at the time the invention was made to alternatively include the isolated enzymes, per se, in the microcapsules of Chang et al. One of ordinary skill in the art would have been motivated to encapsulate isolated enzymes, instead of whole cells, because isolated enzymes can be easily purchased from commercial sources, are less complicated in

terms of biocompatibility, immune reactions and overall safety than genetically modified organisms, isolated enzymes require less effort in storage, packaging and transportation, and compositions comprising isolated enzymes are easier to get approved by the FDA than genetically modified organisms. One would have expected isolated uremic enzymes to successfully breaking down uremic toxins as well as uremic enzymes secreted from transgenic microorganisms because isolated uremic enzymes and secreted uremic enzymes are functional equivalents. Thus, simply because Chang et al and Setala do not specifically teach using isolated enzymes, they do not teach or suggest negative results when isolated enzymes are used. A reference merely not teaching every limitation does not constitute teaching away by that reference. See *In re Grasselli* 713 F.2d 731, 741, 218 USPQ 769, 777 (Fed. Cir. 1983).

In response to the rejections under 103(a) of independent claims 40 and 62 as being unpatentable over Chang et al, in view of Setala, further in view of Yamamoto et al and Shigyo et al, and in light of The Online Medical Dictionary, applicant argues that neither Chang et al nor Setala disclose or suggest transfecting a cell with a uricase gene or a creatininase gene or to the removal of uric acid or creatine. Furthermore, applicants argue that one of ordinary skill in the art, in reading Chang et al, would not be motivated to modify a cell by transfecting it with a uricase gene or a creatininase gene, and thus would not be motivated to combine Chang et al with Setala.

This is not found persuasive because motivation is not required to come from a single reference, but may be expressly or impliedly contained in the prior art or may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law. See MPEP § 2144. In the instant case Setala teaches that uric acid, creatine and urea are all uremic toxins that accumulate in uremic patients (See Setala, col. 3, ln 18-36). Therefore, because all three toxins are known to contribute to uremia, at the time the invention was made it would have been within the general knowledge of one of ordinary skill in the art, due to generally

established scientific principles to treat all causes of a disease when possible, to remove all three uremic toxins. Uricase, creatininase and urease break down uric acid, creatine and urea, respectively, to more dilute compounds which can be excreted in the urine (See The Online Medical Dictionary "Uricase," "Allantoin," "Creatininase," "Creatinine" and "Urea"). Therefore, as stated above, one of ordinary skill in the art would have been motivated to use a cell transfected with uricase, creatininase and urease, encapsulated in the microcapsule taught by Chang et al, in order to aide in the breakdown and removal of all three uremic toxins that accumulate in uremic patients in order to treat uremia.

Applicants further argue that the teachings of Yamamoto and Shigyo do not cure the defects of Chang et al and Setala; they also note that they do not concede that there would be motivation to combine the teachings of Yamamoto and Shigyo with Change and Setala. Yamamoto and Shigyo were relied upon in order to show that it was well within the skill of one of ordinary skill in the art at the time the invention was made to transfect *E.coli* cells with uricase and creatininase genes; thus showing that one skilled in the art would be able to successfully transfect *E.coli* cells with uricase and creatininase for inclusion in the microcapsules of Chang et al.

With regards to applicant "not conceding that there would have been motivation to combine Chang et al and Setala with Yamamoto and Shigyo" as well as applicant "not conceding that any of the definitions from the Online Medical Dictionary are scientifically accurate with respect to one of ordinary skill in the art," these are regarded as arguments of counsel and do not carry any weight without a sustentative evidentiary showing to the contrary. The examiner has provided motivation and definitions as cited above, without specific reasons as to why they are found to be incorrect, they are deemed to be proper.

In response to the rejection under 103(a) of claims 5 and 9 as being unpatentable over Chang et al, in view of Setala, further in view of Yamamoto and Shigyo, and still further in light of the Medical

Dictionary and the Merriam-Webster Online Dictionary (http://www.m-w.com/cgi-bin/dictionary?book=Dictionary&va=enteric, accessed 2/28/05, See PTO-892), applicant argues that because these claims depend directly or indirectly from independent claims 1, 40, 62 and 86, and the premise of the rejections of claims 1, 40, 62 and 86 is incorrect, the rejection of the dependent claims cannot stand. Additionally, applicants state that they do not concede to the accuracy of the Merriam-Webster dictionary, especially from the viewpoint of one of ordinary skill in the art nor do they concede that there would have been any suggestion or motivation in any of Chang et al, Setala, Yamamoto, Shigyo, Online Medical Dictionary, and Merriam-Webster to make the modifications regarding the enteric coating as suggested in the Office Action.

The arguments regarding the rejection of independent claims 1, 40, 62, and 86 have been addressed above. With no additional arguments pertaining to the specific rejections of the limitations of claims 5 and 9, the rejections stand for the reasons of record.

The arguments regarding the lack of motivation or suggestion to combine references as well as the accuracy of the definitions are regarded as arguments of counsel and do not carry any weight without a sustentative evidentiary showing to the contrary. The examiner has provided motivation and definitions as cited above, without specific reasons as to why they are found to be incorrect, they are deemed to be proper.

In response to the rejections under 103(a) of claims 18-21, 46, 67, and 92 as being unpatentable over Chang et al, Setala, Yamamoto, Shigyo, and still further in view of Sparks et al and Wolfe et al, and in light of the Online Medical Dictionary, applicants argue that because these claims depend directly or indirectly from independent claims 1, 40, 62 and 86, and the premise of the rejections of claims 1, 40, 62 and 86 is incorrect, the rejection of the dependent claims cannot stand. Additionally, applicants state that they do not concede that there would have been any suggestion or motivation to combine Chang et al,

Setala, Yamamoto, Shigyo, Online Medical Dictionary, Sparks, and Wolfe in the manner suggested by the Patent Office.

The arguments regarding the rejection of independent claims 1, 40, 62, and 86 have been addressed above. With no additional arguments pertaining to the specific rejections of the limitations of claims 18-21, 46, 67 or 92, the rejections stand for the reasons of record.

The arguments regarding the lack of motivation or suggestion to combine references are regarded as arguments of counsel and do not carry any weight without a sustentative evidentiary showing to the contrary. The examiner has provided motivation and definitions as cited above, without specific reasons as to why they are found to be incorrect, they are deemed to be proper.

In response to the rejections under 103(a) of claims 22-24, 46, 67, and 92 as being unpatentable over Chang et al, Setala, Yamamoto, Shigyo, and still further in view of Smith et al and in light of the Online Medical Dictionary, applicants argue that because these claims depend directly or indirectly from independent claims 1, 40, 62 and 86, and the premise of the rejections of claims 1, 40, 62 and 86 is incorrect, the rejection of the dependent claims cannot stand. Additionally, applicants state that they do not concede that there would have been any suggestion or motivation to combine Chang et al, Setala, Yamamoto, Shigyo, Smith et al, and Online Medical Dictionary, in the manner suggested by the Patent Office.

The arguments regarding the rejection of independent claims 1, 40, 62, and 86 have been addressed above. With no additional arguments pertaining to the specific rejections of the limitations of claims 22-24, 46, 67, and 92, the rejections stand for the reasons of record.

The arguments regarding the lack of motivation or suggestion to combine references are regarded as arguments of counsel and do not carry any weight without a sustentative evidentiary showing to the

contrary. The examiner has provided motivation and definitions as cited above, without specific reasons as to why they are found to be incorrect, they are deemed to be proper.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M Ford whose telephone number is 571-272-2936. The examiner can normally be reached on M-F 7:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651

LEON B. LANKFORD, JR.
PRIMARY EXAMINER